

Structure of the human POSHL1 protein

Fig. 1A

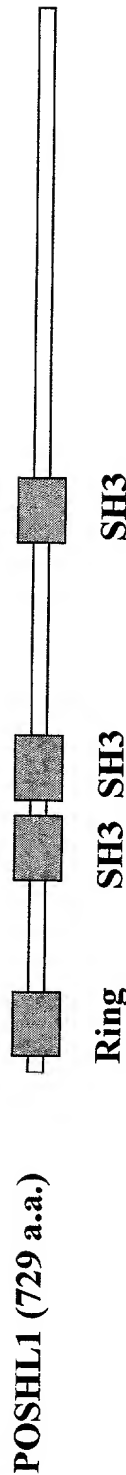


Fig. 1B

Ring Domain

| | | 10 | 20 | 30 | 40 |
|------------|-----|--------------|-----------------|------------------------|------------------|
| | |* |* |* |* |
| consensus | 1 | CPICLEEY | ----LKDPVVLP | CGHT-FCRSCIRKWLESSN | SNTCPIC 41 |
| POSHL1 | 12 | CPVCFEKL | ----DVTAKVLP | CQHT-FCKPCLQRVFKAHK | ELRCPEC 52 |
| 1G25_A | 6 | CPRCCTTKyrnp | SLKLMVNV | CGHT-LCESCVDLLFVRG | --AGNCPEC 49 |
| gi 2145348 | 18 | CPVCLDL | ----FRVPITLM | CGHT-CCKHCLngiv | --ksdNARCPVC 56 |
| gi 2342720 | 91 | CPVCLGLlpk | --nVVIKVLpncMHM | FDEECIGKWLESHa | ---TCPVC 132 |
| gi 2738440 | 111 | CVVCYEN | ----EICIKIQP | CNHFVCKSCFNR | -----LNTCPMC 145 |
| gi 3043558 | 71 | CSICLER | ----YKNPKVLP | CLHT-FCERCLQNYIPAHsl | tLSCPVC 111 |
| gi 3152606 | 28 | CNICFEL | ----AQDPIVTL | CGHL-FCWPCLYRWLHHHsh | SQECPCVC 68 |
| gi 3002588 | 12 | CPVCLERL | ----DASAKVLP | CQHT-FCKRCLLGIVGSRn | -eLRCPEC 52 |
| gi 6226931 | 43 | CPICLDR | ----YKQPKLLP | CQHT-FCYPCLDESCADTLhrn | LKCPEC 83 |

FIG. 1C

SH3 Domain 1

| | 10 | 20 | 30 | 40 | 50 | 60 |
|------------|--|------|----|----|----|----|
| consensus |*.....*.....*.....*..... | | | | | |
| POSHL1 | 1 EGPQVRALYDYTAQDPDELDFKKGDIITVLEKS-----DDGWKGRLG-T | 44 | | | | |
| 1PHT | 126 GVPRAKALCNRYGQNPGLRFNKGDIILRRQL-----DENWYQGEI--N | 168 | | | | |
| gi 3882275 | 4 EGYQYRALYDYKKEREEDIDLHLGDIITVKNKGSvalgfsdggearpeEIGWLNQYNETT | 63 | | | | |
| gi 4176446 | 864 EKLPKAKAVYDFKAQTSKELSFKKGDTVILRKI-----DQNWYEGEHH-- | 906 | | | | |
| gi 2114412 | 509 HRRRAKALLDFERHDDDELGFRKNDIITVSQK-----DEHCWVGELN-- | 551 | | | | |
| gi 2190355 | 994 KLPQVKALYPYTAANDEELSFKKVGDITILEK-----DEGWKKGELN-- | 1035 | | | | |
| gi 4894215 | 244 ENLYATALYPYQASQWHLFFKKDDKIVLLDIKS-----EEGWLKGELN-- | 287 | | | | |
| gi 3158515 | 113 EYGEAVAQYTFKGDLEVELSFRKGEHICLRKV-----NENWYEGRITGT | 157 | | | | |
| gi 3002588 | 383 QKPQCRALFDFDAQSEGELEDKFGTLELVSQI-----DENWYEGRVN-- | 425 | | | | |
| | 135 QLPCAKALYNYEGKEPGLKFSKGDITILRRQV-----DENWYHGEVS-- | 177 | | | | |
| 70 | | | | | | |
| |*.....* | | | | | |
| consensus | 45 GKEGLFPSNYVEEID | 59 | | | | |
| POSHL1 | 169 GISGNFPASSVEVIK | 183 | | | | |
| 1PHT | 64 GERGDFFPGTYVEYIG | 78 | | | | |
| gi 3882275 | 907 GRVGIFPISYVEKLT | 921 | | | | |
| gi 4176446 | 552 GLRGWFPFAKFVEVLID | 566 | | | | |
| gi 2114412 | 1036 QQEGWIPNNYVKEI - | 1049 | | | | |
| gi 2190355 | 288 GKIGYFPASYVEIIA | 302 | | | | |
| gi 4894215 | 158 GRQGIFFASYVQVSR | 172 | | | | |
| gi 3158515 | 426 GKTGLFPVTYVQVLV | 440 | | | | |
| gi 3002588 | 178 GVHGFPTNFVQIIK | 192 | | | | |

FIG. 1D

SH3 Domain 2

| | | | | | | | |
|------------|---------------------|---|---|---------|------|----|----|
| | | 10 | 20 | 30 | 40 | 50 | 60 |
| consensus | |*.....*.....*.....*..... | | | | | |
| 1 | EGPQVRALYDYT | -----A-----QDPDELSFKGDIITVLEKS | -----DD | 35 | | | |
| 188 | PPPLCRALYNFDLrgkdkS | -----ENQDCLTFLKDDIITVISRV | -----DE | 228 | | | |
| 1PHT | 4 | EGYQYRALYDYK | -----K-----EREEDIDLHLGDILTVNKGSLvalgsdggearpeEI | 53 | | | |
| gi 3880771 | 408 | VSPYARAVYDFQ | -----G-----EFENELSFSADEIISLRRRI | -----DA | 442 | | |
| gi 729368 | 153 | EEMLVQALYDFV | -----P-----QESGELDFRRGDVITVTDRS | -----DE | 187 | | |
| gi 1346669 | 458 | KGSQVEALFSYE | -----A-----TQPEDLEFQEGDIILVLSKV | -----NE | 492 | | |
| gi 2961227 | 995 | GPEQARALYDFA | -----A-----ENPDELTFNEGAVVTVINKS | -----NP | 1029 | | |
| gi 2960022 | 3 | QPLVVQAEYSFM | -----G-----SNNDELCFQKGDVITVTQRE | -----DG | 37 | | |
| gi 3002588 | 197 | PPPQCKALYDFE | -----VkdkeADKDCLPFAKDDVLTVIRRV | -----DE | 235 | | |
| gi 3599478 | 1160 | TVGRCRALYDYG | -----A-----QEADELTLREGDVIDVIQK | -----SG | 1193 | | |

| | | | |
|------------|------|--------------------------------|------|
| | | 70 | 80 |
| | |*.....*.....* | |
| consensus | 36 | GWKGRIG-TGKEGLFPSNYVEEID | 59 |
| POSHL1 | 229 | NWAEKGLG-D-KVGIFPILFVEPnl | 251 |
| 1PHT | 54 | GWLNGYNETTGERGDFPGTYVEYIG | 78 |
| gi 3880771 | 443 | EWLEGSIG-SARVGIFPPTSfVQIIV | 466 |
| gi 729368 | 188 | NWNNGEIG--NRKGIFPATYVTPYH | 210 |
| gi 1346669 | 493 | EWLEGECK--GKVGIFPKVFVEDCA | 515 |
| gi 2961227 | 1030 | DWWEDELN--GQRGVFPASVVELIP | 1052 |
| gi 2960022 | 38 | GWWEGLTN--DKTGWFPSPNYVNECK | 60 |
| gi 3002588 | 236 | NWAEGLMA--DKIGIFPISYVEFNS | 258 |
| gi 3599478 | 1194 | EWWEGLTN--GKTGVFPANYVEDI | 1215 |

FIG. 1E

SH3 Domain 3

| | | | | | | | | |
|-------------|-----|--|----|----|----|----|----|-----|
| | | 10 | 20 | 30 | 40 | 50 | 60 | |
| consensus | |*.....*.....*.....*..... | | | | | | |
| POSHL1 | 1 | EGPQVRALYDYTAQDPDELDFKKGDIITVLEKS | | | | | | 43 |
| 1PHT | 381 | SANMFVALHSYSAHGPDELQKGGVRLGKC | | | | | | 424 |
| | 4 | EGYQYRALYDYKKEREEDIDLHLGDILTVNKGSLvalgfsdggearpeEIGWLNGY-NET | | | | | | 62 |
| gi 4322306 | 664 | DLCSYQALYSYVPQNDDELELRDGDIVDMEKC | | | | | | 707 |
| gi 127962 | 107 | LNMPAYVKFNMAEREDLSLIKGTKVIVMEKC | | | | | | 149 |
| gi 7619882 | 126 | GAPHAVALHDFPAEQADDLSLTSGEIVYLLEKI | | | | | | 168 |
| gi 3170194 | 156 | VLYQVVAQHRYSAQGPEDLGRQGDIVDLCEV | | | | | | 198 |
| gi 3002588 | 453 | RPSVYVAIYPYTPRKEDELELRKGEMFLVFERC | | | | | | 496 |
| gi 13324869 | 380 | YLEKVRVLYDYDAAKEDELTLRENAIVYVLKKN | | | | | | 422 |
| gi 488296 | 42 | ANPVWTALFDYEPGSGQDELALRKGRVEVLSRDaai | | | | | | 89 |

70

| | | | | | | | | |
|-------------|-----|---|-----|--|--|--|--|--|
| | |*.....*.....*.....*..... | | | | | | |
| consensus | 44 | TGKEGLFPPSNYVEEID | 59 | | | | | |
| POSHL1 | 425 | TGRVGIFPNPNYVIPIf | 440 | | | | | |
| 1PHT | 63 | TGERGDFPGTYVEYIG | 78 | | | | | |
| gi 4322306 | 708 | TRQFGTFPGNYVKPLY | 723 | | | | | |
| gi 127962 | 150 | -GQVGWFFPSNYVVEEG | 164 | | | | | |
| gi 7619882 | 169 | -NQTGVFPANVVKVIV | 183 | | | | | |
| gi 3170194 | 199 | -GRIGIFPKCFVVPAG | 213 | | | | | |
| gi 3002588 | 497 | TSKIGVFPNGNYVAPVT | 512 | | | | | |
| gi 13324869 | 423 | -GVTGLFPNGNYVVPV | 436 | | | | | |
| gi 488296 | 90 | -GQVGIFPPSNYVSRGG | 104 | | | | | |

Structure of the POSHL1 gene (Chr. 5q32)

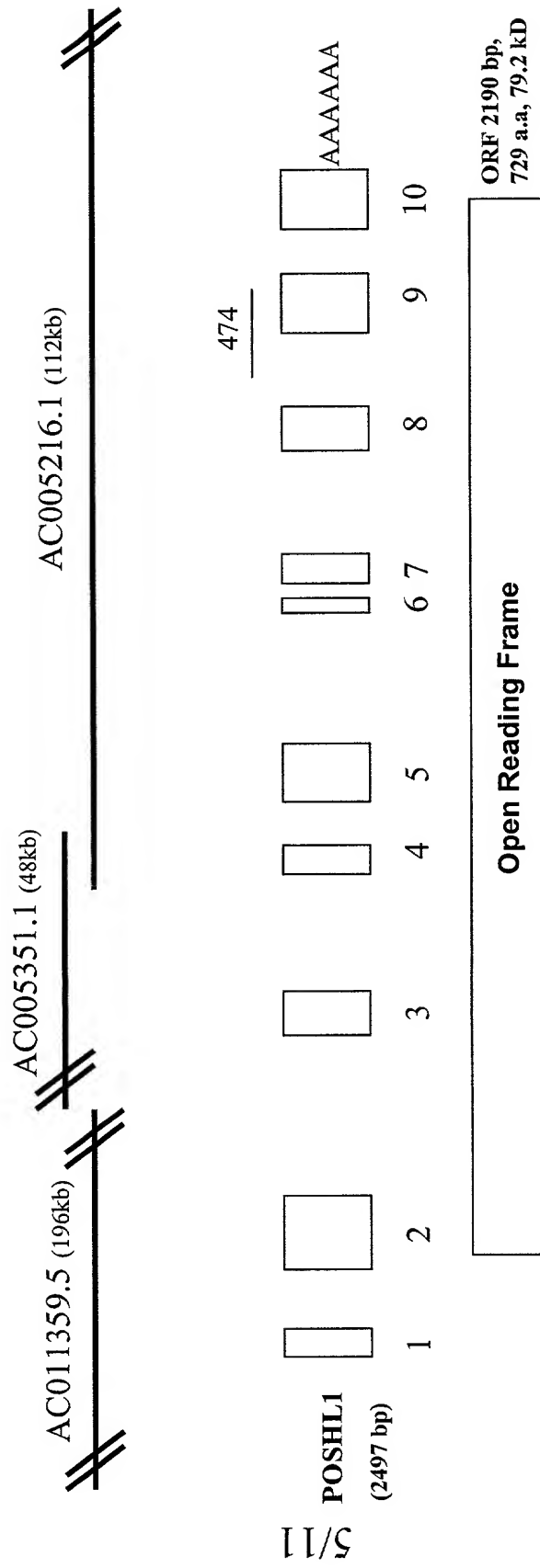


FIG. 2

POSHL1

nt: SEQ ID NO: 1

aa: SEQ ID NO: 3

| | | |
|---|-----------------------------|-----|
| AAAGTTTTTCAAAGCGGTTGGCAGCAGCGGCCTTGAGAGAAAGGAAGCCGGT | | 52 |
| TGGAGGGGCGCAGCGCACCCCTGCTGCGCGGAGGAGGGGGCTGAGCTGAACTC | | 104 |
| AGCAGAAGTTACATGCACAAGGCCAAAAATTCTGACGTTCTCAAGAGACCAGC | | 156 |
| TCTGCCCCCGTGGCTCAACTGACCCTACCATGTGGACGCTGCTCCTCCAGGT | | 208 |
| | M D D L T L L | 7 |
| GGGAACTGGAGTTTTGAAATAAA | ATG GAT GAT TTG ACG TTA CTT | 252 |
| D L L E C P V C F E K L D | | 20 |
| GAT CTT CTG GAG TGC CCT GTG TGC TTT GAG AAG CTC GAT | | 291 |
| V T A K V L P C Q H T F C | | 33 |
| GTC ACA GCC AAA GTC CTC CCT TGC CAG CAC ACC TTC TGC | | 330 |
| K P C L Q R V F K A H K E | | 46 |
| AAA CCA TGT CTA CAG AGG GTT TTC AAG GCC CAC AAA GAG | | 369 |
| L R C P E C R T P V F S N | | 59 |
| CTG CGG TGC CCC GAA TGC AGG ACG CCT GTG TTT TCC AAC | | 408 |
| I E A L P A N L L L V R L | | 72 |
| ATT GAG GCG CTG CCG GCC AAC CTG CTG CTC GTG CGC CTT | | 447 |
| L D G V R S G Q S S G R G | | 85 |
| CTG GAT GGA GTG CGC TCA GGG CAG AGC TCC GGG AGA GGG | | 486 |
| G S F R R P G T M T L Q D | | 98 |
| GGC TCC TTC CGC AGG CCT GGC ACG ATG ACC TTG CAG GAT | | 525 |

FIG. 3

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| G | R | K | S | R | T | N | P | R | R | L | Q | A | 111 |
| GGC | AGG | AAA | AGC | AGG | ACC | AAC | CCC | AGA | CGT | CTG | CAG | GCC | 564 |
| S | P | F | R | L | V | P | N | V | R | I | H | M | 124 |
| AGT | CCT | TTC | CGG | CTA | GTG | CCT | AAT | GTC | AGA | ATC | CAC | ATG | 603 |
| D | G | V | P | R | A | K | A | L | C | N | Y | R | 137 |
| GAT | GGG | GTG | CCT | CGA | GCA | AAG | GCC | TTA | TGC | AAC | TAC | AGA | 642 |
| G | Q | N | P | G | D | L | R | F | N | K | G | D | 150 |
| GGG | CAG | AAT | CCC | GGT | GAC | CTA | AGG | TTT | AAT | AAG | GGA | GAT | 681 |
| I | I | L | L | R | R | Q | L | D | E | N | W | Y | 163 |
| ATC | ATC | CTT | CTC | CGG | AGA | CAG | CTT | GAT | GAG | AAT | TGG | TAC | 720 |
| Q | G | E | I | N | G | I | S | G | N | F | P | A | 176 |
| CAG | GGG | GAA | ATC | AAT | GGC | ATC | AGC | GGG | AAC | TTC | CCA | GCC | 759 |
| S | S | V | E | V | I | K | Q | L | P | Q | P | P | 189 |
| AGC | TCC | GTG | GAA | GTC | ATC | AAG | CAG | CTG | CCC | CAG | CCG | CCC | 798 |
| P | L | C | R | A | L | Y | N | F | D | L | R | G | 202 |
| CCG | CTC | TGC | AGG | GCC | CTC | TAC | AAC | TTC | GAC | CTA | CGA | GGC | 837 |
| K | D | K | S | E | N | Q | D | C | L | T | F | L | 215 |
| AAG | GAC | AAG | AGT | GAG | AAC | CAG | GAT | TGC | CTG | ACC | TTC | CTC | 876 |
| K | D | D | I | I | T | V | I | S | R | V | D | E | 228 |
| AAG | GAC | GAT | ATC | ATC | ACT | GTG | ATC | AGC | CGA | GTG | GAT | GAG | 915 |
| N | W | A | E | G | K | L | G | D | K | V | G | I | 241 |
| AAC | TGG | GCA | GAA | GGC | AAG | TTA | GGA | GAT | AAA | GTA | GGC | ATC | 954 |
| F | P | I | L | F | V | E | P | N | L | T | A | R | 254 |
| TTC | CCT | ATC | TTG | TTT | GTA | GAG | CCA | AAC | CTC | ACC | GCA | AGA | 993 |
| H | L | L | E | K | N | K | G | R | Q | S | S | C | 267 |
| CAC | CTT | TTA | GAG | AAG | AAC | AAA | GGT | CGC | CAG | TCA | TCC | TGC | 1032 |
| T | K | N | L | S | L | V | S | S | S | S | R | G | 280 |
| ACA | AAA | AAC | CTG | TCC | CTG | GTG | TCC | TCG | TCC | TCC | AGA | GGC | 1071 |

FIG. 3

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| N | T | S | T | L | R | R | G | P | G | S | R | R | 293 |
| AAC | ACG | TCT | ACC | CTC | CGT | AGG | GGC | CCA | GGG | TCC | AGG | AGG | 1110 |
| K | V | P | G | Q | F | S | I | T | T | A | L | N | 306 |
| AAG | GTG | CCT | GGG | CAG | TTT | TCC | ATC | ACA | ACA | GCC | TTG | AAC | 1149 |
| T | L | N | R | M | V | H | S | P | S | G | R | H | 319 |
| ACT | CTC | AAC | CGG | ATG | GTC | CAT | TCT | CCT | TCA | GGG | CGC | CAT | 1188 |
| M | V | E | I | S | T | P | V | L | I | S | S | S | 332 |
| ATG | GTA | GAG | ATC | AGC | ACC | CCA | GTG | CTC | ATC | AGC | TCC | AGC | 1227 |
| N | P | S | V | I | T | Q | P | M | E | K | A | D | 345 |
| AAC | CCC | TCT | GTG | ATC | ACC | CAG | CCC | ATG | GAG | AAA | GCA | GAC | 1266 |
| V | P | S | S | C | V | G | Q | V | S | T | Y | H | 358 |
| GTT | CCT | TCC | AGC | TGT | GTG | GGA | CAG | GTC | AGC | ACT | TAT | CAC | 1305 |
| P | A | P | V | S | P | G | H | S | T | A | V | V | 371 |
| CCC | GCA | CCT | GTC | TCT | CCA | GGA | CAT | TCC | ACA | GCC | GTG | GTC | 1344 |
| S | L | P | G | S | Q | Q | H | L | S | A | N | M | 384 |
| AGT | CTG | CCT | GGC | TCC | CAG | CAA | CAC | CTC | TCA | GCG | AAC | ATG | 1383 |
| F | V | A | L | H | S | Y | S | A | H | G | P | D | 397 |
| TTT | GTA | GCC | CTG | CAC | TCC | TAC | TCA | GCC | CAT | GGA | CCC | GAT | 1422 |
| E | L | D | L | Q | K | G | E | G | V | R | V | L | 410 |
| GAG | CTG | GAC | CTG | CAA | AAG | GGA | GAA | GGC | GTC | AGG | GTC | CTG | 1461 |
| G | K | C | Q | D | G | W | L | R | G | V | S | L | 423 |
| GGG | AAG | TGC | CAG | GAC | GGC | TGG | CTC | AGG | GGC | GTC | TCC | TTG | 1500 |
| V | T | G | R | V | G | I | F | P | N | N | Y | V | 436 |
| GTC | ACC | GGG | CGA | GTC | GGC | ATC | TTC | CCA | AAC | AAT | TAC | GTC | 1539 |
| I | P | I | F | R | K | T | S | S | F | P | D | S | 449 |
| ATC | CCC | ATT | TTC | AGA | AAG | ACC | TCT | AGT | TTT | CCA | GAC | TCC | 1578 |
| R | S | P | G | L | Y | T | T | W | T | L | S | T | 462 |
| CGG | AGC | CCT | GGT | CTC | TAC | ACC | ACA | TGG | ACG | TTA | TCC | ACC | 1617 |

FIG. 3

9/11

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| S | S | V | S | S | Q | G | S | I | S | E | G | D | 475 |
| TCC | TCT | GTG | TCC | TCC | CAA | GGC | AGC | ATT | TCA | GAA | GGT | GAT | 1656 |
| P | R | Q | S | R | P | F | K | S | V | F | V | P | 488 |
| CCA | CGG | CAA | AGC | CGT | CCC | TTC | AAA | TCC | GTC | TTT | GTG | CCC | 1695 |
| T | A | I | V | N | P | V | R | S | T | A | G | P | 501 |
| ACT | GCC | ATA | GTC | AAC | CCC | GTG | AGA | AGC | ACA | GCC | GGC | CCT | 1734 |
| G | T | L | G | Q | G | S | L | R | K | G | R | S | 514 |
| GGG | ACT | TTA | GGA | CAA | GGG | TCT | CTT | CGG | AAA | GGG | CGG | AGC | 1773 |
| S | M | R | K | N | G | S | L | Q | R | P | L | Q | 527 |
| AGC | ATG | AGA | AAG | AAT | GGA | TCC | CTG | CAG | AGA | CCC | CTC | CAG | 1812 |
| S | G | I | P | T | L | V | V | G | S | L | R | R | 540 |
| TCC | GGG | ATC | CCC | ACT | CTC | GTG | GTA | GGC | TCC | CTC | AGA | CGC | 1851 |
| S | P | T | M | V | L | R | P | Q | Q | F | Q | F | 553 |
| AGC | CCC | ACC | ATG | GTC | CTT | CGG | CCT | CAG | CAG | TTC | CAA | TTC | 1890 |
| Y | Q | P | Q | G | I | P | S | S | P | S | A | V | 566 |
| TAC | CAG | CCA | CAG | GGG | ATC | CCC | TCC | TCC | CCC | TCA | GCC | GTG | 1929 |
| V | V | E | M | G | S | K | P | A | L | T | G | E | 579 |
| GTG | GTG | GAG | ATG | GGG | TCC | AAG | CCT | GCC | CTC | ACG | GGG | GAG | 1968 |
| P | A | L | T | C | I | S | R | G | S | E | A | R | 592 |
| CCC | GCC | CTC | ACG | TGC | ATC | AGC | AGG | GGC | AGT | GAG | GCC | CGG | 2007 |
| T | H | S | A | A | S | S | L | I | M | E | D | K | 605 |
| ACC | CAC | TCC | GCG | GCC | AGC | TCC | CTC | ATT | ATG | GAA | GAC | AAA | 2046 |
| E | I | P | I | K | S | E | P | L | P | K | P | P | 618 |
| GAA | ATC | CCC | ATC | AAG | AGT | GAG | CCT | CTG | CCA | AAA | CCG | CCC | 2085 |
| A | S | A | P | P | S | I | L | V | K | P | E | N | 631 |
| GCA | TCT | GCC | CCA | CCA | TCC | ATC | CTG | GTG | AAA | CCA | GAA | AAC | 2124 |
| S | R | N | G | I | E | K | Q | V | K | T | V | R | 644 |
| TCA | AGA | AAT | GGC | ATC | GAA | AAG | CAA | GTC | AAA | ACC | GTG | AGA | 2163 |

FIG. 3

10/11

| | | | | | | | | | | | | | |
|--|-----|-----|-----|-----|-----|-----|-----|---------------------|-----|-----|-----|-----|------|
| F | Q | N | Y | S | P | P | P | T | K | H | Y | T | 657 |
| TTT | CAG | AAT | TAC | AGC | CCT | CCT | CCC | ACC | AAA | CAT | TAC | ACC | 2202 |
| | | | | | | | | | | | | | |
| S | H | P | T | S | G | K | P | E | Q | P | A | T | 670 |
| TCC | CAT | CCC | ACC | TCC | GGA | AAG | CCT | GAA | CAG | CCA | GCC | ACC | 2241 |
| | | | | | | | | | | | | | |
| L | K | A | S | Q | P | E | A | A | S | L | G | P | 683 |
| CTC | AAG | GCG | TCC | CAG | CCT | GAA | GCA | GCG | TCC | TTG | GGC | CCA | 2280 |
| | | | | | | | | | | | | | |
| E | M | T | V | L | F | A | H | R | S | G | C | H | 696 |
| GAG | ATG | ACC | GTC | CTA | TTT | GCC | CAC | CGA | AGT | GGC | TGC | CAC | 2319 |
| | | | | | | | | | | | | | |
| S | G | Q | Q | T | D | L | R | R | K | S | A | L | 709 |
| TCC | GGA | CAG | CAG | ACA | GAC | CTC | CGG | AGA | AAG | TCA | GCT | CTT | 2358 |
| | | | | | | | | | | | | | |
| A | K | A | T | T | L | V | S | T | A | S | G | T | 722 |
| GCC | AAG | GCC | ACA | ACC | CTG | GTG | TCC | ACT | GCC | TCA | GGC | ACG | 2397 |
| | | | | | | | | | | | | | |
| Q | T | V | F | P | S | K | * | | | | | | 730 |
| CAG | ACC | GTG | TTT | CCC | AGC | AAA | TGA | ACCTACGGGTGACTTTTCC | | | | | 2440 |
| | | | | | | | | | | | | | |
| TAGACCCCAAAGAGGTGAATTGCATTTAAATACAGTCTGCCTCCACTAAAAA | | | | | | | | | | | | | 2492 |
| | | | | | | | | | | | | | |
| AAAAA | | | | | | | | | | | | | 2497 |

FIG. 3

RT-PCR Analysis of POSHL1 Expression

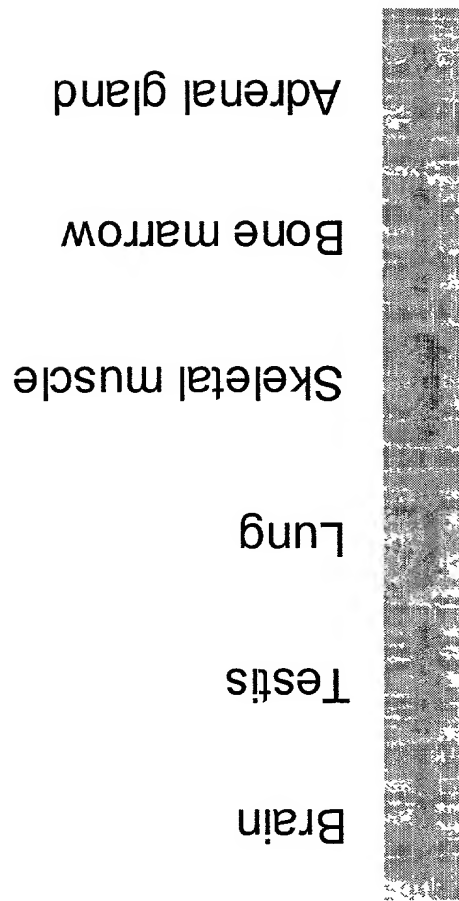


FIG. 4